DN PREV199497368234
TI Requirements for tumor necrosis factor-alpha and interleukin-1 in limb ischemia/reperfusion injury and associated lung injury.
AU Seekamp, Andreas; Warren, Jeffrey S.; Remick, Daniel G.; Till, Gerd O.; Ward, Peter A.
CS Dep. Pathol., Univ. Mich. Med. Sch., 1301 Catherine St., Box 0602, Ann Arbor, MI 48109-0602 USA
SO American Journal of Pathology, (1993) Vol. 143, No. 2, pp. 453-463. ISSN: 0002-9440.
DT Article
LA English
AB Ischemia in rat hind limbs followed by reperfusion results in local as well as remote organ (lung) injury characterized by increased vascular permeability (125I-labeled bovine serum albumin leakage) and hemorrhage (51Cr-labeled rat erythrocytes extravasation) in skeletal muscle and lung, together with an associated increased tissue content of myeloperoxidase, reflecting neutrophil accumulation. Within 60 minutes of reperfusion following ischemia, tumor necrosis factor-alpha (TNF-alpha), interleukin-1 (IL-1), and IL-6 plasma levels increased significantly, reaching maximum levels after 2 hours of reperfusion Polyclonal antibodies to TNF-alpha and IL-1 provided significant protection against vascular **injury** in both **muscle** and lung. These results were confirmed by the use of soluble **TNF**-alpha **receptor** and IL-1 receptor antagonist. In rat lungs following ischemia and reperfusion, there was immunohistochemical evidence of E-selectin expression in the lung vasculature; this expression was blocked by treatment of animals with anti-TNF-alpha. These data indicate that both local (bind limb) and remote (lung) organ injury after ischemia/reperfusion requires participation of TNF-alpha and IL-1. The cytokines may, in part, be involved in the up-regulation of endothelial adhesion molecules.

L14 ANSWER 19 OF 19 CA COPYRIGHT 2001 ACS
AN 113:4041 CA
TI Studies on cytokines in Kawasaki disease III. Serum .gamma.-interferon levels in relation to tumor necrosis factor and interleukin 2 receptor in patients with Kawasaki disease involving coronary artery lesions
AU Matsubara, Tomoyo
CS Sch. Med., Juntendo Univ., Tokyo, Japan
SO Arerugi (1990), 39(2-1), 118-23
CODEN: ARERAM; ISSN: 0021-4884
DT Journal
LA Japanese
AB Serum levels of .gamma.-interferon (IFN-.gamma.) were detd. by a sandwich RIA in patients with Kawasaki disease (KD), measles, streptococcal infection, anaphylactoid purpura, and various types of vasculitis. The level of IFN-.gamma. was increased during the acute phase of KD and measles. Serum levels of tumor necrosis factor (TNF) and interleukin 2 receptor (IL-2R) were also measured in patients with KD. In KD patients with coronary artery lesions (CAL), the percentage of cases pos. for TNF (.gtoreq.10 units/mL), IL-2R (.gtoreq.1056 units/mL), and IFN-.gamma. (.gtoreq.0.3 units/mL) was higher than that in patients without CAL.

=> d his

(FILE 'HOME' ENTERED AT 16:14:40 ON 04 MAY 2001)

FILE 'CA, USPATFULL, BIOSIS, MEDLINE, DRUGU, EMBASE' ENTERED AT 16:15:58 ON 04 MAY 2001
L1 45274 S ETANERCEPT OR INFLIXIMAB OR (TNF OR TUMOR NECRO? FACTOR OR TU

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L2       382920 S RETINA? OR (OPTIC OR OCULA? OR MACULA?)(2A)(NERVE? OR
NEURITI
L3          387 S L1 AND L2
L4          313 S L1(L)L2
L5          313 S L3 AND L4
L6          257 DUP REM L5 (56 DUPLICATES REMOVED)
L7           39 S L1(10A)L2
L8           60 S L1(20A)L2
L9           36 DUP REM L8 (24 DUPLICATES REMOVED)
L10      148433 S (MUSCLE? OR MUSCULAR)(2A)(DISORDER? OR INFLAMMAT? OR INJUR?
O
L11         236 S L1 AND L10
L12         178 S L1(L)L10
L13          37 S L1(20A)L10
L14          19 DUP REM L13 (18 DUPLICATES REMOVED)
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=> s (muscle? or muscular)(2a)(disorder? or inflammat? or injur? or activ? or
dystroph?) or polymyositit or dermatomyositis

   3 FILES SEARCHED...
L10     148433 (MUSCLE? OR MUSCULAR)(2A)(DISORDER? OR INFLAMMAT? OR INJUR? OR
               ACTIV? OR DYSTROPH?) OR POLYMYOSITIT OR DERMATOMYOSITIS

=> s l1 and l10

L11         236 L1 AND L10

=> s l1(l)l10

L12         178 L1(L) L10

=> s l1(20a)l10

L13          37 L1(20A) L10

=> dup rem l13

PROCESSING COMPLETED FOR L13
L14          19 DUP REM L13 (18 DUPLICATES REMOVED)

=> d 1-19 bib,ab


L14  ANSWER 1 OF 19  CA  COPYRIGHT 2001 ACS
AN   134:80816  CA
TI   Combination of tumors necrosis factor (TNF) antagonists and
cyclooxygenase
     2 (COX-2) inhibitors for the treatment of inflammation
IN   Keane, J. Timothy
PA   Pharmacia Corporation, USA
SO   PCT Int. Appl., 86 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2001000229      A1   20010104       WO 2000-US16292  20000626
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-141238    P    19990624
OS   MARPAT 134:80816
AB   The invention provides combinations of a TNF antagonizing agent and a
     COX-2 inhibiting agent for treating inflammatory disease in a mammal.
RE.CNT  12
```

RE
(1) Aggarwal, B; US 5795967 A 1998 CA
(3) Feng, L; US 5731343 A 1998 CA
(4) Gordon, G; WO 9816227 A 1998 CA
(6) Lorenz, H; EXP OPIN INVEST DRUGS 2000, P1479 CA
(7) Moreland, L; ANN INTERN MED 1999, V130(6), P478 CA
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 19 USPATFULL
AN 2001:10539 USPATFULL
TI TNT inhibitors for the treatment of neurological disorders
IN Tobinick, Edward L., 100 UCLA Medical Plaza, Suite 205, Los Angeles, CA,
United States 90024-6903
PI US 6177077 20010123
AI US 1999-476643 19991231 (9)
RLI Continuation-in-part of Ser. No. US 1999-275070, filed on 23 Mar 1999, now patented, Pat. No. US 6015557 Continuation-in-part of Ser. No. US 1999-256388, filed on 24 Feb 1999, now abandoned
DT Utility
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Sutton, Ezra
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 853
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is disclosed for inhibiting the action of TNF for treating neurological conditions in a human by administering a TNF antagonist for
reducing the inflammation of neuronal tissue or the neuromuscular junction of a human, or for modulating the immune response affecting neuronal tissue or the neuromuscular junction of a human by administering to the human a therapeutically effective dosage level of a
TNF antagonist. The TNF antagonist is selected from the group consisting
of etanercept, infliximab, pegylated soluble TNF receptor Type I (PEGsTNF-R1), other agents containing soluble TNF receptors, CDP571 (a humanized monoclonal anti-TNF-alpha antibody), other monoclonal anti-TNF-alpha antibodies, TNF-alpha converting enzyme inhibitors and D2E7 (a human anti-TNF mAb) for reducing the inflammation of neuronal tissue or the neuromuscular junction of a human, or for modulating the immune response affecting neuronal tissue or the neuromuscular junction of a human.

L14 ANSWER 3 OF 19 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-11073 DRUGU T E
TI Mononeuritis secondary to rheumatoid arthritis responds to etanercept.
AU Richter C; Wanke L; Steinmetz J; Reinhold Keller E; Gross W L
LO Bad Bramstedt, Ger.
SO Rheumatol. (39, No. 12, 1436-37, 2000) 5 Ref. ISSN: 1462-0324
AV Rheumaklinik, Oskar-Alexander Strasse, 24576 Bad Bramstedt, Germany.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB A case of mononeuritis secondary to rheumatoid arthritis (RA) that responded to etanercept was reported in a letter. The patient had been treated with hydroxychloroquine (HCQ), salazosulphapyridine (ASA), azathioprine, gold preparations, MTX, peroral cyclophosphamide, MTX + ASA
+ HCQ and MTX + cyclosporin A. Cyclosphosphamide and cyclosporin were stopped because of side effects. Etanercept was added to MTX, ASA, and prednisolone with rapid improvement of the joints within a few wk, and

almost complete remission; only mild signs of residual axonal neuropathy.

L14 ANSWER 4 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2000:513469 BIOSIS
DN PREV200000513469
TI Elevation of serum soluble **tumour necrosis factor receptors** in patients with polymyositis and **dermatomyositis**.
AU Shimizu, T.; Tomita, Y. (1); Son, K.; Nishinarita, S.; Sawada, S.; Horie, T.
CS (1) 30-1 Oyaguchikamimachi, Itabashi-ku, Tokyo, 173-8610 Japan
SO Clinical Rheumatology, (2000) Vol. 19, No. 5, pp. 352-359. print.
ISSN: 0770-3198.
DT Article
LA English
SL English
AB The aim of the study was, to examine the relationship between serum levels of soluble tumour necrosis factor receptors (sTNF-R) and the gene expression of two types of receptor for TNF (TNF-R), a 55 kDa **receptor** (**TNF**-R1) and a 75 kDa **receptor** (**TNF**-R2), in peripheral blood mononuclear cells (PBMC) from patients with polymyositis and **dermatomyositis** (PM/DM). Soluble **tumour necrosis factor receptor** 1 (sTNF-R1) and soluble **tumour necrosis factor receptor** 2 (sTNF-R2) levels in sera from patients were measured by enzyme-linked immunosorbent assay. Expression of TNF-R1 and TNF-R2 mRNAs in PBMC was analysed by Northern blotting. Serum sTNF-R1 and sTNF-R2 levels were elevated significantly in 25 patients with active-stage PM/DM, compared to those in 18 patients with inactive-stage PM/DM and 32 normal controls. Serum concentrations of sTNF-R1 and sTNF-R2 were correlated with PM/DM disease activity. TNF-R1 gene expression was enhanced in freshly isolated PBMC from patients with active-stage PM/DM. In contrast, TNF-R2 mRNA was expressed constitutively in patients with active-stage PM/DM and in normal controls. The expression of TNF-R1 and TNF-R2 mRNAs in PBMC and elevation of their soluble forms in the sera of patients with active-stage PM/DM suggest increased proteolytic cleavage of cell surface TNF-R from PBMC in patients with active-stage PM/DM, and that sTNF-R may regulate TNF-alpha-mediated muscle fibre damage in PM/DM.

L14 ANSWER 5 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:377422 BIOSIS
DN PREV200000377422
TI **TNF receptor** subtypes in airway smooth **muscle** stimulate stress-**activated** protein kinases.
AU McFarlane, Shona M. (1); Jupp, Orla J. (1); Cobban, Hannah J. (1); Nixon, Graeme F. (1); MacEwan, David J. (1)
CS (1) Dept Biomedical Sciences, Institute Medical Sciences, University of Aberdeen, Aberdeen, AB25 2ZD UK
SO Scandinavian Journal of Immunology, (June, 2000) Vol. 51, No. Supplement 1, pp. 66. print.
Meeting Info.: 8th International TNF Congress, Conference on Tumor Necrosis Factor and Related Molecules Scientific Advances and Medical Applications Trondheim, Norway May 14-18, 2000
ISSN: 0300-9475.
DT Conference
LA English
SL English

L14 ANSWER 6 OF 19 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-04640 DRUGU T S

TI Experience with **etanercept** in chronic juvenile **dermatomyositis** (JDM): preliminary results.
AU Miller M L; Mendez E; Klein Gitelman M S; Pachman L M
LO Chicago, Ill., USA
SO Arthritis Rheum. (43, No. 9, Suppl., S380, 2000) 1 Tab. 1 Ref.
CODEN: ARHEAW ISSN: 0004-3591
AV No Reprint Address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB **Etanercept** treatment was well tolerated but only modestly effective among 4 patients with chronic juvenile **dermatomyositis**. **Etanercept** is a **TNF-receptor** agonist. (conference abstract: American College of Rheumatology 64th Annual Scientific Meeting and Association of Rheumatology Health Professionals 35th Annual Scientific Meeting, Philadelphia, Pennsylvania, USA, 2000).

L14 ANSWER 7 OF 19 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-03890 DRUGU T
TI **Etanercept** is effective in the treatment of polymyositis and **dermatomyositis** which is refractory of conventional therapy including steroids and other disease-modifying agents.
AU Saadeh C K
LO Amarillo, Tex., USA
SO Arthritis Rheum. (43, No. 9, Suppl., S193, 2000)
CODEN: ARHEAW ISSN: 0004-3591
AV No Reprint Address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB **Etanercept** was well tolerated and highly effective in 3 women and a girl with refractory polymyositis and **dermatomyositis**. **Etanercept** is a soluble **TNF-receptor** agonist. (conference abstract: American College of Rheumatology 64th Annual Scientific Meeting and Association of Rheumatology Health Professionals 35th Annual Scientific Meeting, Philadelphia, Pennsylvania, USA, 2000).

L14 ANSWER 8 OF 19 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-03891 DRUGU T
TI Anti-**TNF-blockade** with **infliximab** (Remicade) in polymyositis and **dermatomyositis**.
AU Hengstman G; van den Hoogen F; van Engelen B; Barrera P; Netea M; van de Putte L
LO Nijmegen, Neth.
SO Arthritis Rheum. (43, No. 9, Suppl., S193, 2000)
CODEN: ARHEAW ISSN: 0004-3591
AV No Reprint Address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB **Infliximab** (Remicade; Schering-Plough) treatment was well tolerated and effective in 2 patients with polymyositis (PM) and **dermatomyositis** (DM). **Infliximab** is a chimeric anti-TNF monoclonal antibody. (conference abstract: American College of Rheumatology 64th Annual Scientific Meeting and Association of Rheumatology Health Professionals 35th Annual Scientific Meeting, Philadelphia, Pennsylvania, USA, 2000).

L14 ANSWER 9 OF 19 CA COPYRIGHT 2001 ACS
AN 132:192734 CA
TI Human muscle damage impairs insulin-signal transduction at the level of IRS-1, PI3-kinase and akt-kinase: potential role for TNF-alpha inhibition

of insulin action in skeletal muscle
AU Del Aguila, Luis F.
CS Pennsylvania State Univ., University Park, PA, USA
SO (1999) 139 pp. Avail.: UMI, Order No. DA9940837
From: Diss. Abstr. Int., B 2000, 60(8), 3868
DT Dissertation
LA English
AB Unavailable

L14 ANSWER 10 OF 19 CA COPYRIGHT 2001 ACS DUPLICATE 2
AN 130:280112 CA
TI A sustained rat model for studying the long-lasting catabolic state of sepsis
AU Breuille, Denis; Voisin, Laure; Contrepois, Michel; Arnal, Maurice; Rose, Francis; Obled, Christiane
CS Clintec Technologies, Velizy-Villacoublay, 78140, Fr.
SO Infect. Immun. (1999), 67(3), 1079-1085
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Most animal models of sepsis induced high mortality or early recovery and do not mimic the long-lasting catabolic state obsd. in patients. The purpose of this study is to develop a model of sepsis which reproduces these disorders, esp. the long-lasting muscle wasting. This report summarizes our observations in a series of seven expts. using this model with rats to study the route of live Escherichia coli administration, dose of bacteria, reproducibility of the model, bacterial count in tissues, comparison of injection of live or dead bacteria, metabolic perturbations linked to infection, and potential role of tumor necrosis factor alpha (TNF-.alpha.) in muscle wasting. After i.v. infection, animals were anorexic and the catabolic state was long-lasting: body wt. loss for 2 to 3 days followed by a chronic wasting state for several days. Liver, spleen, lung protein content, and plasma concn. of .alpha.2-macroglobulin were increased 2 and 6 days after infection. At 6 days, muscle protein content was substantially (-40%) reduced. The plasma TNF-.alpha. level measured 1.5 h after infection correlated with body wt. loss obsd. 9 days later. The **inhibition** of **TNF**-.alpha. secretion by administration of pentoxifylline 1 h before infection reduced **muscle** wasting and **activation** of proteolysis at day 2 and abolished them at day 6. This septic model mimics in rats the prolonged protein metab. alterations and muscle atrophy characteristics of infected patients and thus is useful for studying the impact of nutritional support on outcome.
RE.CNT 40
RE
(1) Aarden, L; Eur J Immunol 1987, V17, P1411 CA
(3) Ash, S; Clin Sci 1989, V76, P659 CA
(5) Breuille, D; Am J Physiol 1993, V265, PE660 CA
(6) Breuille, D; Clin Sci 1994, V86, P663 CA
(7) Cory, A; Cancer Commun 1991, V3, P207 CA
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 1999:147512 BIOSIS
DN PREV199900147512
TI Attenuation of skeletal **muscle** ischemia/reperfusion **injury** by **inhibition** of **tumor necrosis factor**.
AU Gaines, Gregory C.; Welborn, Burress, III; Moldawer, Lyle L.; Huber, Thomas S. (1); Harward, Timothy R. S.; Seeger, James M.
CS (1) Dep. Surg./Univ. Fla. Coll. Med., PO Box 100286, Gainesville, FL 32610-0286 USA

SO Journal of Vascular Surgery, (Feb., 1999) Vol. 29, No. 2, pp. 370-376. ISSN: 0741-5214.
DT Article
LA English
AB Purpose: Tumor necrosis factor alpha (TNF-alpha) has been shown to play a role in pulmonary injury after lower-extremity ischemia/reperfusion (I/R).
However, its role in direct skeletal muscle injury is poorly understood. The hypothesis that endogenous TNF production contributes to skeletal muscle injury after hindlimb I/R in rats was tested. Methods: juvenile male Sprague-Dawley rats underwent 4 hours of bilateral hindlimb ischemia and 4 hours of reperfusion (IR) or sham operation (SHAM). A subset was treated with a soluble **TNF receptor** I construct (STNFRI, 10 mg/kg) 1 hour before ischemia (PRE) or at reperfusion (POST). Direct skeletal **muscle injury** (SMII) and **muscle** endothelial capillary permeability (MPI) were quantified by means of Tc99 pyrophosphate and 1125 albumin uptake. Pulmonary neutrophil infiltration and hepatocellular injury were assessed by means of myeloperoxidase content (MPO) and aspartate aminotransferase (AST) concentrations, respectively. Serum TNF bioactivity was measured with the WEHI bioassay. Results: Hindlimb I/R (IR vs SHAM) resulted in a significant ($P < .05$) increase in the SMII (0.52 +- 0.06 vs 0.07 +- 0.01) and MPI (0.35 +- .04 vs 0.06 +- 0.01). Pretreatment with STNFRI (PRE vs IR) significantly ameliorated both SMII (0.30 +- 0.05 vs 0.52 +- 0.06) and MPI (0.23 +- 0.02 vs 0.35 +- 0.04), whereas treatment at reperfusion (POST vs IR) had no effect. Hindlimb I/R (IR vs SHAM) resulted in both significant pulmonary neutrophil infiltration (MPO 16.4 +- 1.06 U/g vs 11.3 +- 1.4 U/g) and hepatocellular injury (AST 286 +- 45 U/mL vs 108 +- 30 U/mL), but neither was inhibited by pretreatment with STNFRI before ischemia. Detectable levels of TNF were measured during ischemia in a significantly higher percentage of the IR group compared with SHAM (9 of 12 vs 3 of 12), and the maximal TNF values were also significantly greater (51.1 +- 12.6 pg/mL vs 5.5 +- 2.9 pg/mL). No TNF was detected in any treatment group during reperfusion nor after administration of the STNFRI.
Conclusion: Acute hindlimb IR initiates a systemic TNF response during the ischemic period that is partly responsible for the associated skeletal muscle injury.

L14 ANSWER 12 OF 19 MEDLINE DUPLICATE 4
AN 1999327950 MEDLINE
DN 99327950 PubMed ID: 10399751
TI Immunolocalization of tumor necrosis factor-alpha and its receptors in inflammatory myopathies.
AU De Bleecker J L; Meire V I; Declercq W; Van Aken E H
CS Neurology Department, University Hospital, Gent, Belgium.. jan.debleecker@rug.ac.be
SO NEUROMUSCULAR DISORDERS, (1999 Jun) 9 (4) 239-46.
Journal code: BJS; 9111470. ISSN: 0960-8966.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990913
Last Updated on STN: 19990913
Entered Medline: 19990901
AB Adhesion molecule upregulation occurs in inflammatory myopathies, and is one of the myriad functions of tumor necrosis factor-alpha (TNF-alpha). TNF-alpha acts via two different **receptors** of 55 (**TNF**-R55) and 75 kD (TNF-R75). We immunolocalized **TNF**-alpha and its

receptors in polymyositis, inclusion body myositis and **dermatomyositis**. In each myopathy, TNF-alpha was detected in macrophages, in myonuclei in regenerating muscle fibers, and freely dispersed in endomysial or perimysial connective tissue. Many endothelial cells in dermatomyositis expressed TNF-alpha. TNF-R55 was strongly expressed on myonuclei of regenerating muscle fibers. TNF-R75 was increased on endothelial cells in the midst of inflammatory infiltrates in each myopathy, and on perifascicular and perimysial endothelia, remote from inflammatory foci in dermatomyositis. Possible TNF-alpha-mediated effects include: increased transendothelial cell trafficking, activation of T/B cells and macrophages, induction of MHC-I gene products, and focal muscle fiber atrophy. In dermatomyositis, the upregulated TNF-R75, via its consensus elements for transcription factors, may be involved in endothelial cell degeneration. Strong TNF-R55 expression on regenerating myonuclei is consistent with a role of TNF-alpha and TNF-R55 in muscle regeneration.

L14 ANSWER 13 OF 19 CA COPYRIGHT 2001 ACS
AN 130:152428 CA
TI TNF inhibits insulin induced STAT5 activation in differentiated mouse muscle cells pmi28
AU Storz, Peter; Doppler, Heike; Wernig, Anton; Pfizenmaier, Klaus; Mulle, Gertraud
CS Institute of Cell Biology and Imnmunology, University of Stuttgart, Stuttgart, D-70569, Germany
SO FEBS Lett. (1998), 440(1,2), 41-45
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB Tumor necrosis factor (TNF) plays a central role in the state of insulin resistance leading to type II diabetes. The authors describe here the crosstalk of TNF with insulin signaling cascades in the mouse muscle cell line pmi28. TNF downregulated insulin-induced insulin receptor kinase activity and insulin-induced activation of the transcription factor STAT5.
The authors' results provide evidence that the inhibitory crosstalk between TNF and insulin in skeletal muscle cells comprises an interference with the expression of STAT5 regulated genes which may play an important role in the manifestation and/or progression of insulin resistance in muscle cells.
RE.CNT 29
RE
(1) Bader, D; J Cell Biol 1982, V95, P763 CA
(3) Chen, J; Proc Natl Acad Sci USA 1997, V94, P2295 CA
(4) Cohen, B; Science 1996, V274, P1185 CA
(5) Darnell, J; Science 1997, V277, P1630 CA
(6) Ewart, H; FEBS Lett 1998, V425, P179 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 1997:362404 BIOSIS
DN PREV199799654337
TI Elevated serum levels of neopterin in adult patients with polymyositis/dermatomyositis.
AU Samsonov, M. Y.; Nassonov, E. L.; Tilz, G. P.; Geht, B. M.; Demal, U.; Gurkina, G. T.; Shtutman, V. Z.; Guseva, A. G.; Wachter, H.; Fuchs, D. (1)
CS (1) Inst. Med. Chem. Biochem., Univ. Innsbruck, Fritz-Pregl Str. 3, A-6020 Innsbruck Austria
SO British Journal of Rheumatology, (1997) Vol. 36, No. 6, pp. 656-660.

ISSN: 0263-7103.
DT Article
LA English
AB We determined serum concentrations of neopterin, soluble **tumour necrosis factor** (55 kDa) **receptor** (sTNF-R) and soluble interleukin-2 receptor (sIL-2R) in plasma of 44 patients with polymyositis (PM)/**dermatomyositis** (DM), including 15 patients with primary PM, 13 patients with primary DM, and 16 patients with myositis and systemic sclerosis in overlap. Concentrations of neopterin, sTNF-R and sIL-2R were measured using commercially available immunoassays.

Serum neopterin was increased in 35 of 44 PM/DM patients (80%), sTNF-R in 14 (32%) and sIL-2R in 18 (41%) patients, respectively. There were significant correlations between serum neopterin and sTNF-R, sIL-2R and erythrocyte sedimentation rate (all P lt 0.001). Neopterin, as well as sTNF-R and sIL-2R, did not correlate with clinical (neuromuscular and activities of daily living scores) and laboratory (creatine kinase levels) manifestations of myositis. Increased serum levels of neopterin were associated with non-muscular manifestations of PM/DM. In conclusion, serum neopterin appears to be a useful laboratory marker for ongoing immune activation and global disease activity in PM/DM.

L14 ANSWER 15 OF 19 CA COPYRIGHT 2001 ACS DUPLICATE 6
AN 127:189482 CA
TI Exogenous human recombinant interleukin-10 attenuates hindlimb ischemia-reperfusion injury
AU Engles, Robert E.; Huber, Thomas S.; Zander, Dani S.; Hess, Philip J.; Welborn, M. Burress; Moldawer, Lyle L.; Seeger, James M.
CS Department of Surgery, University of Florida College of Medicine, Gainesville, FL, 32610-0286, USA
SO J. Surg. Res. (1997), 69(2), 425-428
CODEN: JSGRA2; ISSN: 0022-4804
PB Academic
DT Journal
LA English
AB Proinflammatory cytokines have been found to mediate part of the local and distant organ injury after ischemia and reperfusion (I/R). The anti-inflammatory cytokine interleukin-10 (IL-10) **inhibits** both **TNF**-.alpha. and IL-1, and we hypothesized that exogenous human IL-10 may decrease lung and soleus **muscle injury** after hindlimb I/R. Male Sprague-Dawley rats were randomly assigned to I/R; I/R + IL-10 (10 .mu.g i.v.), SHAM; or SHAM + IL-10 (10 .mu.g i.v.). Bilateral hindlimb ischemia was produced by tourniquet occlusion for 4 h and all animals were sacrificed after 4 h of reperfusion or at comparable times for the SHAMs. Soleus muscle cellular injury was detd. by uptake of 99Tc pyrophosphate while soleus muscle capillary permeability, and lung capillary permeability were assessed by uptake of 125I-labeled albumin. Soleus muscle and lung neutrophil infiltration were measured with the myeloperoxidase assay. Serum samples were assessed for TNF -.alpha. prodn. with the WEHI bioassay. Hindlimb I/R caused significant soleus muscle cellular injury, soleus muscle capillary injury, lung capillary injury, and lung neutrophil infiltration. Pretreatment with exogenous IL-10 significantly reduced soleus muscle capillary permeability and also reduced soleus muscle cellular injury, but not to a statistically significant degree. IL-10 administration also reduced pulmonary capillary permeability despite significantly increased lung neutrophil infiltration.

Elevated TNF -.alpha. levels were found in 66% (4/6) rats in the I/R group

vs. 30% (3/10) rats in the I/R + IL-10 group. Exogenous IL-10 attenuates both local and distant organ injury after hindlimb I/R potentially independent of neutrophil infiltration.

L14 ANSWER 16 OF 19 CA COPYRIGHT 2001 ACS DUPLICATE 7
AN 128:33610 CA
TI TNF inhibits myogenesis and downregulates the expression of myogenic regulatory factors myoD and myogenin
AU Szalay, Katalin; Razga, Zsolt; Duda, Erno
CS MTA Biological Research Center, Institute Biochemistry, Szeged, H-6701, Hung.
SO Eur. J. Cell Biol. (1997), 74(4), 391-398
CODEN: EJCBDN; ISSN: 0171-9335
PB Wissenschaftliche Verlagsgesellschaft mbH
DT Journal
LA English
AB The presence of TNF and other inflammatory cytokines and their receptors is detected during embryonic development, but the knowledge about the role of these proteins in differentiation and development is very limited. Tumor necrosis factor (TNF) modulates the synthesis and activity of a no. of transcriptional proteins that regulate the activity of tissue specific genes, therefore it may play a role in normal development. Since its synthesis is upregulated by stress and infections, it may also participate in the induction of pathol. developmental processes and malformation. The effect of TNF was investigated in an in vitro differentiation system using C2 myoblasts. This inflammatory cytokine exerted a pos. effect on the early steps of the process: it enhanced the proliferation and aggregation of myoblast cells. In contrast, **TNF** strongly **inhibited** the expression of the myogenic transcription factors (myoD and myogenin), which are known to be responsible for upregulated **activity** of **muscle** specific genes (like the genes of the myofilament proteins), and blocked the synthesis of mRNAs of myogenic differentiation markers (like skeletal a-actin, myosin heavy and light chains). As a result, these cells did not synthesize myofilament proteins and the organization of myofilaments did not take place in TNF-treated myoblasts.

L14 ANSWER 17 OF 19 DRUGU COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-16248 DRUGU T
TI Dermatomyositis responding to pentoxifylline.
AU Person J R
LO Auburn, Mass., USA
SO Br.J.Dermatol. (134, No. 3, 593, 1996) 13 Ref.
CODEN: BJDEAZ ISSN: 0366-2845
AV Department of Dermatology, Fallon Clinic Inc., Auburn, MA 01501, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB In a letter to the journal, the Authors report the beneficial effects of pentoxifylline (PF) in a 60-yr-old woman with probable dermatomyositis. Previously, lichen sclerosus affecting the vulva, perineum and perianal region had been treated with clobetasol ointment and p.o. doxycycline, with moderate response. When lesions developed on her hand, changing to PF rapidly normalized elevated creatine kinase (CK); eruptions of her hand almost completely cleared. CK rose when PF was stopped. It was suggested that PF may be effective in **dermatomyositis** by virtue of its fibrinolytic or viscosity lowering properties or by **inhibiting TNF**-alpha.

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